

REMARKS

A. Regarding the Amendments

Claims 2 and 3 have been amended as set forth in the attached Exhibit A, "Version With Markings To Show Changes Made". As amended, the claims are supported by the specification and the original claims. Applicants submit that the amendments to the claims are for clarity and should not be construed as amendments affecting patentability under *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 234 F.3d 558, 56 USPQ2d 1865 (Fed. Cir. 2000) (en banc). Thus, upon entry of the amendments, claims 2-11 will be pending.

B. Claim Objections

Claim 3 was objected for referring to a claimed sequence by reference to a figure number, rather than identification of an entered sequence. The Examiner's attention is respectfully drawn to the claims, as amended, wherein the occurrences of "Figure 1" in the claims has been replaced with the language "SEQ ID NO:1" or "SEQ ID NO:2," as appropriate. Accordingly, the claims no longer refer to the sequence by its figure number. Removal of the objection is therefore respectfully requested.

C. Rejection Under 35 U.S.C. § 112

Applicants respectfully traverse the rejection of claims 2-11 under 35 U.S.C. § 112, first paragraph, as containing subject matter allegedly not described in the Specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the invention at the time of filing of the Application. In particular, it is alleged in Paper No. 14 that claims 2-11 are directed to any molecule that could be identified as encoding "GDF-16" and do not set forth any particular structural features or structural characteristics of GDF-16. Applicants respectfully disagree.

Applicants respectfully submit that the claims, as pending, do include structural features or characteristics of the claimed sequence. Structurally, the claimed enzyme must be a polynucleotide that encodes a GDF-16 polypeptide as set forth in SEQ ID NO:2; SEQ ID NO:1, where the Ts can also be Us; nucleic acid sequences complementary to SEQ ID NO:1; and fragments of the above, where the fragments are at least 15 bases in length and will identify a DNA sequence which encodes a GDF-16 polypeptide of SEQ ID NO: 2 by hybridization; or SEQ ID NO:1.

The Examiner has noted that the GDF-16 polypeptide and polynucleotide of the invention is "closely related" to human BMP-17 and BMP-18 as shown in US 6,027,917. In fact, BMP-17 and -18 appear to be human homologs of a murine protein called Lefty. Applicants note that Lefty-1 was the probe utilized to clone the GDF-16 polynucleotide of the invention (see Example 1). (The nucleotide and amino acid sequences of murine Lefty are described in Zhou et al., *Nature*, 361:543-547 (1993)). The murine Lefty gene has been described as being expressed in the mouse node during gastrulation. A related human protein, designated endometrial bleeding associated factor [EBAF] was published in Kothapelli et al., *J. Clin. Invest.*, 99:2342-2350 (1997)). Thus, the GDF-16 of the invention is a confirmed member of not only the GDF family of proteins, but also of the well known bone morphogenic proteins (BMPs). One of skill in the art would immediately recognize that as a family member, GDF-16 inherently possesses activity including stimulation of growth and formation of bone (as has been shown for the BMP family).

It is alleged in Paper No. 14 that "there is no way to determine what variations would be tolerated without altering them," or "what fragments...would possess the same defining characteristics." The Examiner's attention is respectfully drawn to the application at page 7, lines 2-4, which states that "all degenerate nucleotide sequences are included in the invention as long as the amino acid sequence of GDF-16 polypeptide encoded by the nucleotide sequence is functionally unchanged." The claims with regard to the fragments, recite fragments of SEQ ID NO:1, where the Ts can also be Us or nucleic acid sequences complementary to SEQ ID NO:1,

where the fragments are at least 15 bases in length and will identify a DNA sequence which encodes a GDF-16 polypeptide of SEQ ID NO: 2 by hybridization.

As the specification discloses the specific structural characteristics of the claimed sequences, claims 2-11 meet the written description requirement of 35 U.S.C. §112, first paragraph. Accordingly, withdrawal of the rejection is requested.

Applicants respectfully traverse the rejection of claims 2-11 under 35 U.S.C. § 112, first paragraph, as allegedly non-enabled for a genus identifiable a "GDF-16" or fragments of the disclosed species. However, the Examiner has acknowledged that the specification is enabled for the polynucleotides encoded by SEQ ID NO:1 (Paper No. 14, page 3). It is noted that the claims are not directed to any GDF-16, but to a polynucleotides sequence encoding GDF-16, as set forth in SEQ ID NO: 2 (claim 1); SEQ ID NO:1, where T can also be U; nucleic acid sequences complementary to SEQ ID NO: 1; or SEQ ID NO:1 itself. One of skill in the art would be able to identify any of the claimed polynucleotides. Where claim 3 recites fragments, it is specifically fragments of SEQ ID NO:1, where T can also be U or fragments of nucleic acid sequences complementary to SEQ ID NO:1, which are at least 15 bases in length and will hybridize to DNA that encodes a GDF-16 polypeptide of SEQ ID NO:2.

Additionally, it is stated in Paper No. 14 that "Applicant has not described the characteristics of this molecule that one of skill in the art could predictably identify other sequences encoding "GDF-16." As set forth above, the claims are not directed to any sequences that encode GDF-16. All of the claimed polynucleotides are recited as having particular structural characteristics, which are readily identifiable by one of skill in the art. As such, one of skill in the art would be able to practice the present invention. Therefore, claims 2-11 meet the enablement requirement of 35 U.S.C. §112, first paragraph. Accordingly, the removal of the rejection is requested.

Applicants respectfully traverse the rejection of claims 3-11 under 35 U.S.C. §112, second paragraph as allegedly indefinite for failing to point out and distinctly claim the subject matter of the invention, as the term "GDF-16" is referred to in the claims, rather than a specific sequence. The Examiner's attention is respectfully drawn to amended claim 2. As amended, the claim recites "the growth differentiation factor-16 (GDF-16) polypeptide as set forth in SEQ ID NO:2." The amended claim specifies that the polypeptide encoded by the claimed polynucleotide sequence is a growth differentiation factor and is SEQ ID NO:2.

Additionally, claim 3 is rejected as allegedly indefinite for recitation of the term "selectively hybridizes" and for referring to a Figure Number, rather than a sequence identification number. The Examiner's attention is respectfully directed to the amended claims. As amended, claim 3 no longer contains the term "selectively hybridizes," and no longer refers to a Figure number 1, but includes SEQ ID Nos: 1 or 2, where appropriate.

Therefore, claims 2-11 meet the definiteness requirement of 35 U.S.C. §112, second paragraph. Accordingly, it is respectfully requested that the rejections be withdrawn.

In re Application of:
Lee et al.
Application No.: 09/485,045
Filed: May 12, 2000
Page 7

PATENT
Attorney Docket No.: JHU1440-1

CONCLUSION

In summary, for the reasons set forth herein, Applicants maintain that claims 2-11 clearly and patentably define the invention, respectfully request that the Examiner reconsider the various grounds set forth in the Office Action, and respectfully request the allowance of the claims which are now pending.

If the Examiner would like to discuss any of the issues raised in the Office Action, Applicant's representative can be reached at (858) 677-1456. Please charge any additional fees, or make any credits, to Deposit Account No. 50-1355.

Respectfully submitted,

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Lisa A. Haile, J.D., Ph.D.
Registration No. 38,347
Telephone: (858) 677-1456
Facsimile: (858) 677-1465

GRAY CARY WARE & FREIDENRICH LLP
4365 Executive Drive, Suite 1100
San Diego, California 92121-2133

USPTO Customer Number 28213

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Exhibit A - Page 1



PATENT

Attorney Docket No.: JHU1440-1

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS

Claims 2 and 3 have been amended as follows:

2. (Amended) An isolated polynucleotide sequence encoding the growth differentiation factor-16 (GDF-16) polypeptide [of claim 1] as set forth in SEQ ID NO: 2.
3. (Amended) An isolated polynucleotide selected from the group consisting of:
 - a) [FIGURE 1] SEQ ID NO: 1, wherein T can also be U;
 - b) nucleic acid sequences complementary to [FIGURE 1] SEQ ID NO: 1;
 - c) fragments of a) or b) that are at least 15 bases in length and that will [selectively hybridize to] identify a DNA sequence which encodes [the] a GDF-16 polypeptide of [FIGURE 1] SEQ ID NO: 2 by hybridization; and
 - d) SEQ ID NO: 1.